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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/619,149	07/14/2003	Sanjeev Kumar (Mendiratta)	213-0086US	8546

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EXAMINER	
KOSSON, ROSANNE	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/619,149	KUMAR (MENDIRATTA), SANJEEV	
	Examiner	Art Unit	
	Rosanne Kosson	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II, claims 10-16, in the reply filed on August 18, 2004 is acknowledged. Also acknowledged is Applicant's cancellation of claims 1-9 and 17-27. Thus, claims 10-16 are pending for examination.

Information Disclosure Statement

The Information Disclosure Statement filed on October 17, 2003 indicates that six pages of PTO-1449 forms are attached. Pages 2-6 of the PTO-1449 forms are not, however, present in Applicant's file. Applicant is requested to send a copy of the missing pages to the Office in order to have the cited references considered. The pages may be sent by fax to the following number: 703-872-9306.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-16 are rejected under 35 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described the specification such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of

the claimed invention. Specifically, claim 10 recites any modified anti-angiogenic serpin fragment that is covalently linked to a polymer. This claim language encompasses a multitude of possible fragments, including fragments neither contemplated nor disclosed by the specification as filed. Applicant has not provided any structure or description for any fragments of an anti-angiogenic serpin. Applicant has also not provided any guidance for preparing such fragments. In view of the great breadth of the claimed subject matter, combined with the fact that the specification as filed provides a description of only complete serpins, such as PEDF, it is clear that at the time of filing the application, Applicant possessed those only those compounds actually set forth in the specification. Thus, a holding of failure to meet the written description requirement is required.

Claim 10-16 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an anti-angiogenic serpin covalently linked to a polymer, does not reasonably provide enablement for any fragment of an anti-angiogenic serpin covalently linked to polymer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. As discussed above with respect to the written description requirement, claim 10 recites any fragment of an anti-angiogenic serpin covalently linked to polymer. As also discussed above, this claim language encompasses a multitude of possible fragments of anti-angiogenic serpins, including compounds neither contemplated nor disclosed by the specification as filed

and for which Applicant has provided no guidance as to the structure of the claimed fragments or as to methods for their preparation. In view of the great extent of the claimed subject matter, combined with the fact that the specification as filed provides a description of only a limited amount of guidance (examples of how to make and use modified PEDF), is clear that in order to practice the scope of the claimed subject matter, the artisan of ordinary skill would have expected to have undertaken essentially a trial and error process. Such a process clearly amounts to undue experimentation. Because the specification provides no guidance as to the fragments to be made and the methods by which such fragments would be made, the skilled artisan clearly would have expected to have to experiment unduly to practice the claimed invention. In sum, undue experimentation would be required to practice the invention as claimed due to the quantity of experimentation necessary; limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art; predictability or unpredictability in the art; and breadth the claims (In re: Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). A holding of non-enablement is, therefore, clearly required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Henkin et al. (WO 02/26782) in view of Chader et al. (US 5,840,686), Kovesdi et al. (US 6,753,321), Mast et al. (Biol Chem Hoppe-Seyler 371(Suppl.):101-109, 1990) and Woodle et al. (US 5,013,556). Henkin discloses anti-angiogenic protein fragments, such as the kringle 5 fragment of plasminogen (K5) covalently linked to a polyethylene glycol (PEG), a polyalkylene glycol or a bi-polymer composed of P and L or P and X regions, in which the L and X regions may be composed of C_1 to C_{10} alkylene moieties and P is a water-soluble polymer. The polymer may have a molecular weight of about 20,000 (see p. 1, last paragraph; p. 2, 2^d full paragraph and last paragraph; p. 3, 1st and 3^d paragraphs; and pp. 7-10 and 15). Henkin does not disclose covalently linking polyethylene glycol, or similar polymers, to PEDF.

Mast discloses coupling PEG to serpins to increase plasma retention times with no significant decrease in activity due to coupling PEG to the serpins (see p. 101, 2d paragraph; and Results on pp. 103-106). Mast does not disclose covalently linking PEG to PEDF, but does disclose that, because PEGylated serpins have desirable properties as pharmaceuticals, it is also desirable to produce large quantities of these compounds for treating a large number of patients. Therefore, serpins that can be produced recombinantly are well suited to this formulation (see p. 107, last paragraph).

Chader discloses the nucleic acid sequence and the amino acid sequence for the human serpin PEDF and recombinant production of human PEDF in *E. coli*. Chader also discloses that PEDF is involved in vascular and degenerative diseases and in maintenance of normal retinas (see column 1, lines 25-53; column 28, lines 46-50; and

columns 31-36). Kovesdi discloses that PEDF is an anti-angiogenic agent (see column 5, line 55, to column 6, line 16).

One of ordinary skill in the art at the time that the invention was made would have recognized that the PEDF protein, in particular the recombinant PEDF protein, disclosed in Chader would have been covalently linked to PEG, or a similar polymer, such as a bipolymer, as disclosed by Henkin, because Henkin and Mast teach that covalently linking an anti-angiogenic protein to PEG, or a similar polymer, improves the serum retention time and the stability of the anti-angiogenic protein, which result in improved pharmaceutical properties.

Woodle discloses that PEG activated with a sulfonyl group may be used to couple PEG to primary amines (see Figure 4; column 4, lines 34-53; and column 7, line 53, to column 8, line 3). One of ordinary skill in the art would have recognized that the sulfonyl-activated PEG would have been used to covalently link PEG to PEDF because Woodle discloses that sulfonyl-activated PEG may be used to couple PEG to a wide variety of amines and that the resulting products are particularly blood-stable. Thus, the skilled artisan would have been motivated to modify the processes of Mast and Henkin for producing PEG-coupled anti-angiogenic serpins by using the PEG coupling process of Woodle for the advantages disclosed in Woodle.

Accordingly, a holding of obviousness is required. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-

2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rosanne Kosson
Examiner
Art Unit 1651

FRANCISCO PRATS
PRIMARY EXAMINER

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2004-09-02